

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 07 SEP 2005

WIPO

PCT

Applicant's or agent's file reference		FOR FURTHER ACTION		See Form PCT/PEA/416
International application No. PCT/EP2004/005800		International filing date (day/month/year) 28.05.2004		Priority date (day/month/year) 03.06.2003
International Patent Classification (IPC) or national classification and IPC A61K7/48				
Applicant UNILEVER PLC et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 5 sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in Item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand 21.12.2004		Date of completion of this report 06.09.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Simon, F Telephone No. +49 89 2399-2083		



INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/005800

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-3, 7-11

as originally filed

4-6

received on 21.12.2004 with letter of 06.12.2004

Claims, Numbers

1-8

received on 21.12.2004 with letter of 06.12.2004

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/005800

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-8
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-8
Industrial applicability (IA)	Yes: Claims	1-8
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/005800

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

The present application relates to a skin lightening composition comprising 0.1 - 50 % by weight of extracts of plants from the genera *Symplocos* and *Rubia*; the extract of *Symplocos* being selected from *Symplocos recemosa*, *Symplocos paniculata*, *Symplocos cochinchinensis* or mixtures thereof; the extract of *Rubia* being *Rubia cordifolia* (see independent claim 1).

1 Reference is made to the following documents cited in the search report:

- D1 : EP 1 284 134 A (2003-02-19)
- D2 : DATABASE WPI AN 2003-614018, XP002296363
& KR 2003 033 723 A (2003-05-01)
- D3 : GB 2 304 050 A (1997-03-12)
- D4 : PAJ, vol. 2000, no. 24 (2001-05-11)
& JP 2001 192317 A (2001-07-17)
- D5 : FR 2 483 226 A (1981-12-04)
- D6 : PAJ, vol. 2003, no. 06 (2003-06-03)
& JP 2003 055184 A (2003-02-26)
- D7 : WO 02/47656 A (2002-06-20)
- D7a: EP 1 352 640 (2003-10-15) - intermediate document
- D8 : US 6 068 834 A (2000-05-30)
- D9: DATABASE WPI, AN 2001-461626, XP002296364
& JP 2001 163755 A (2001-06-19)

2 Novelty (Art. 33(1)(2) PCT)

None of D1 to D9 directly and unambiguously discloses a composition in accordance with present claim 1.

- ▶ Present claim 1 is distinguished over each of D2, D7, D5 and D9 by claiming a composition comprising an extract of any of *Symplocos recemosa*, *Symplocos paniculata*, *Symplocos cochinchinensis* or *Rubia cordifolia*.
- ▶ Present claim 1 is distinguished over each of D1, D4 and D6 by claiming a composition comprising an extract of *Rubia cordifolia*.

- Present claim 1 is distinguished over each of D3 and D8 by claiming a composition comprising an extract of *Symplocos recemosa*, *Symplocos paniculata* or *Symplocos cochinchinensis*.

Therefore the subject matter of amended claim 1 is novel over each of D1 to D9.

3 Inventive step (Art. 33(1)(3) PCT)

D1 addresses the problem of providing drugs for inhibiting sebum secretion without exhibiting side effects (D1, page 2, lines 22-23); D2 addresses the problem of providing an agent for preventing cancer and aging (see D2, abstract); D3 addresses the problem of providing an agent for accelerating the healing of chronic skin problems like psoriasis, eczema and lichen planus (see D3, page 1). D4 addresses the problem of providing matrix metalloproteinase inhibitors which are capable of sustaining elastic skin, preventing skin aging and sustaining fresh skin conditions (see abstract); D5 addresses the problem of providing a natural colorant for application in cosmetic preparations (see D5, page 1, lines 8-11). Thus, none of the documents D1 to D5 addresses the problem of providing cosmetic composition with skin lightening efficacy.

D7 and D9 describe compositions useful in promoting skin whitening (see D7, paragraph 0001 and D9, abstract) but do not disclose or suggest the use of extracts of the genus *Symplocos* or that of *Rubia cordifolia* to promote skin lightening. The document D6 discloses skin compositions for preventing liver spots and freckles. These compositions prevent hyperpigmentation generated by melanin and are skin lightening compositions. D6 therefore is considered as the closest prior document. The compositions described in D6 comprise a plant extract obtained from a *Symplocos* plant, in particular RAKEMOSA (i.e. *Symplocos recemosa*, see D6, [0009]). Aqueous solutions comprising *Symplocos recemosa* are disclosed in [0018] to [0021]. A cream comprising 0.1% of *Symplocos recemosa* is disclosed in example 1 (see [0024]), a gel comprising 1.0% of *Symplocos recemosa* is disclosed in example 4 (see [0029]), a bath composition comprising 5.0% of *Symplocos recemosa* is disclosed in example 7 (see [0032]). Other compositions comprising said extract are shown in examples 2 and 3 (see [0026], [0028]). The skin whitening function of this kind of plant extracts is mentioned in [0001], [0008]-[0009] and [0058]. The present compositions differ from those disclosed in D6 in that they additionally comprise an extract of *Rubia* being *Rubia cordifolia*. The use of *Rubia cordifolia* in

skin lightening compositions is known from D8; in this document, *Rubia cordifolia* is disclosed as anti-inflammatory agent (see D8, col 43, lines 36-42).

Thus, the mere juxtaposition of the teaching of D6 and D8 leading to the association of plant extracts from the genus *Symplocos* and *Rubia cordifolia* simply having at the same time a lightening and an anti-inflammatory effect without producing any surprising and unexpected working inter-relationship would be obvious to the skilled man.

The present application refers to a synergistic effect obtained by combining extracts of the plants *Symplocos* and *Rubia*. However, a synergistic effect cannot be deduced from table 1 on page 9, since the melanin content measured for the combination *Symplocos* and *Rubia* is higher (i.e. worse) than that measured for *Symplocos* alone. If the Applicant were able to show with accurate and comprehensive comparative data that each one of the combinations *extract of Symplocos recemosa*, *Symplocos paniculata* and *Symplocos cochinchinensis* with an extract of *Rubia cordifolia* shows synergistic skin lightening benefits over an extract of either plant alone inventive step could be acknowledged.

- 12 -

CLAIMS

1. A cosmetic skin lightening composition, comprising 0.1 - 50 % by weight of extracts of plants from the genera *Symplocos* and *Rubia*; the extract of *Symplocos* being selected from *Symplocos recemosa*, *Symplocos paniculata*, *Symplocos cochinchinensis* or mixtures thereof; the extract of *Rubia* being *Rubia cordifolia*.
2. The cosmetic skin lightening composition of claim 1, additionally comprising 0.1 - 10 % by weight of a sunscreen.
3. The cosmetic skin lightening composition of claim 1 or claim 2, further comprising 0.1 - 10 % by weight of one or more skin whitening agents.
4. The cosmetic skin lightening composition of any preceding claim, wherein the extract of *Symplocos* is *Symplocos recemosa*.
5. The cosmetic skin lightening composition of any of claims 2 to 4, wherein the sunscreen is selected from 4-tertiary butyl-4'-methoxy dibenzoylmethane, 2-ethyl hexyl methoxy cinnamate, micronized titanium dioxide, or micronized zinc oxide.
6. The cosmetic skin lightening composition of any of claims 3 to 5, wherein the skin whitening agent is niacin, niacinamide or a precursor thereof.

- 13 -

7. The cosmetic skin lightening composition of any preceding claim further comprising extracts of *Glycyrrhiza*, *Coriandum*, *Acorus* or mixtures thereof.

5 8. The cosmetic skin lightening composition of any preceding claim wherein the *Symplocos* or *Rubia* is extracted from the bark of the plant.

10

- 4 -

obtain skin bleaching effect and JP11021228 (Kanebo, 1999) discloses *Glycyrrhiza* as an anti-inflammatory agent.

US6455057 (Elizabeth Arden, 2002), discloses a skin care composition comprising petroselinic acid and/or derivatives thereof; a phenolic compound and/or mixtures thereof; and a dermatologically acceptable vehicle for treating wrinkles and soothing sensitive skin. However, they disclose coriander seed oil as a source of petroselinic acid.

However, none of the prior art teaches the skin lightening and protection against damaging effects of ultraviolet radiation by using the extracts of *Symplocos* or *Rubia* and cosmetic compositions comprising them.

It is the object of the invention to provide a synergistic cosmetic composition comprising skin lightening actives selected from plant sources.

It is another object of the invention to provide a synergistic cosmetic composition that will provide protection against the damaging effects of ultra violet radiation by the use of actives from natural sources.

It is yet another object of the invention to provide a synergistic cosmetic composition that will provide skin lightening with out requiring the use of chemical actives.

Summary of the Invention:

According to the present invention there is provided a cosmetic skin lightening composition comprising 0.1 - 50% by weight of extracts of plants from the genera *Symplocos* and

- 5 -

- *Rubia*; the extract of *Symplocos* being selected from *Symplocos recemosa*, *Symplocos paniculata*, *Symplocos cochinchinensis* or mixtures thereof; the extract of *Rubia* being *Rubia cordifolia*.

- 5 *Symplocos*, is a genus belonging to the family Symplocaceae, commonly available in India. It has several species of which *S. recemosa*, *S. paniculata* and *S. cochinchinensis* are the species for use in the composition.
- 10 *Rubia*, is a genus belonging to the family Rubiaceae of which *R. cordifolia*, commonly available in India is the species for use in the composition.

According to the preferred aspect of the present invention
15 the cosmetic skin lightening composition comprises 0.1 to 10% by weight of a sunscreen.

The plant parts used in the composition may be selected from any part of the plant but preferably from the stem, bark,
20 leaves, flowers, or roots. It is particularly preferred that the bark of the plant is used.

The extract is prepared using any suitable solvent and particularly preferred solvent is water.

25

Detailed Description of the Invention:

It is an essential aspect of the present invention that the plant extracts of *Symplocos* and *Rubia* are incorporated in the cosmetic composition. However, other plant extracts from
30 *Glycyrrhiza*, *Coriandum*, *Acorus* and useful conventional ingredients may be added to the composition.

- 6 -

The conventional ingredients may be in the nature of sunscreens, other skin lightening agents chosen from natural or other synthetic sources, moisturizers, humectants, benefit agents, perfumes etc.

5

The composition of the invention may optionally comprise from 0.1 to 10%, preferably 0.5 to 5% by weight of one or more skin whitening agents. The skin whitening agent is preferably chosen from niacin, niacinamide or a precursor

10 thereof that is capable of releasing niacinamide on the skin. Niacinamide is the amide of niacin and is also known as

nicotinamide or pyridine-3-carboxylic acid. An example of a compound which is a niacinamide precursor is niacinamide ascorbate. Other suitable skin whitening agents include

15 extracts of placenta, hydroquinone and derivatives (eg. arbutin), kojic acid, dicarboxylic acids (azelaic acid, sebacic acid), represented by the formula $\text{HOOC}-(\text{C}_x\text{H}_y)-\text{COOH}$ where $x=4$ to 20 and $y=6$ to 40, ascorbic acid and derivatives thereof, hydroxy acids (lactic acid, glycolic acid, malic
20 acid, tartaric acid etc), ferulic acid, retinol and derivatives or any other known skin whitening compounds.

The sunscreens used may be organic or inorganic in nature and are preferably chosen from 4-tertiary butyl-4'-methoxy

25 dibenzoylmethane, available under the trade name PARSOL 1789 ex Givaudan, 2-ethyl hexyl methoxy cinnamate, available under the trade name PARSOL MCX ex Givaudan or mixtures of the two